

Clean Copy of Amended Specification

Page 1, insert paragraph before paragraph 1:

c4 This application is a national stage 371 application of PCT/AU98/00795, filed September 23, 1998 from which priority is claimed.

Page 6, third full paragraph:

c5 **Figures 1A-1C** provide the nucleotide and amino acid (single letter code) sequence of 2.2412. Numbers refer to distances in base pairs. Ankyrin-type repeat sequences are underlined. An additional repeat sequence is indicated by italics. This stop codon is represented by an asterisk. The original cDNA clone 2.2412 isolated by the two hybrid screen spans nucleotides 694-2664 of this sequence.

Page 9, second and third full paragraphs:

c6 A novel cDNA of 1971 bp. designated 2.2412. was also isolated. This clone encoded a polypeptide of 657 amino acids in frame with the Gal4 DNA-BD. The cDNA did not contain a stop codon. and this. together with the Northern analysis described below. indicated that it was incomplete. This DNA fragment was therefore used as a probe to screen a human placental cDNA library (5' STRETCH PLUS. Clontech. in λ gt10). This resulted in the isolation of two clones. designated clone 8 and clone 12. Clone 8 was approximately 2 kb and overlapped the original 2.2412 clone by 900 bp at the 3' end. This clone provided the carboxy-terminal end of the 2.2412 protein sequence(Figures 1A-1C). Clone 12 was approximately 3.5 kb and to date has

provided an additional 692 bp of sequence information in the 5' direction. The nucleotide and protein sequence for 2.2412 provided by these overlapping clones is shown in Figures 1A-1C. Since a 5' initiation codon has yet to be identified the coding sequence still appears to be incomplete.

Database searches using the 2.2412 cDNA sequence revealed significant homology with a large number of proteins containing ankyrin-like repeats. These sequences were first identified as homologous regions between certain cell cycle regulatory proteins and the Drosophila protein Notch (Breedon and Nasmyth. Nature 329. 651-654. 1987) but subsequently they have been identified in a wide variety of other proteins where they are thought to function in protein-protein interactions (Bork. Proteins 17. 363-374 1993). Subsequent analysis of the protein sequence identified 18 consecutive ankyrin repeats and an additional repetitive element (Figures 1A-1C). The ankyrin repeat region is followed by a stretch of approximately 40 amino acids rich in serine residues. The remaining C-terminal region has a relatively high content of charged amino acids.

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cDNAs encoding the full length and – and C-terminal regions of the original 2.2412 cDNA clone (nucleotides 694-2664, 694-1614 and 1615-2664 of the sequence shown in Figures 1A-1C, respectively) were cloned into the vector pGEX4T2 (Pharmacia). The full length construct was generated by subcloning from the pACT2 clone as a NdeI fragment, whereas the shorter constructs were synthesized by directional cloning of PCR products. The corresponding GST-fusion proteins were purified from IPTG-induced bacterial cultures using glutathione-agarose beads (Smith and Johnson, Gene 67, 31-40, 1988). These immobilized fusion proteins